UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/916,257	07/30/2001	Alla Shapiro	7505.100	1216

7590 06/03/2004

Karen L. Orzechowski
Liniak, Berenato, Longacre & White, LLC
Suite 240
6550 Rock Spring Drive
Bethesda, MD 20817

EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/916,257	SHAPIRO, ALLA	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-9,18-25 and 30-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-9, 18-25, 30-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 13, 2004 has been entered.

Status of the Claims

Claims 2-9, 18-25, 30-39 are pending in this application. In the first five pages of the Amendment submitted on February 13, 2004, Applicant incorrectly refered to claims 10-17, 26-28 as claims that are withdrawn. However, on the May 12, 2003 filing, Applicant has clearly canceled these claims; therefore, claims 10-17, 26-28 are no longer pending in this application. Thus, claims 2-9, 18-25, 30-39 are hereby acted on their merits.

Any rejection that is not addressed in this Office Action is considered withdrawn to avoid redundancy or are further moot in view of the new grounds of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 32, 37, 20-25 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "normally functioning cells" in claim 32 is a relative term which renders the claim indefinite. The term "normally functioning cells" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 37 lines 4 and 5 recite the limitation "said radiation produced by said radioactive substance." There is insufficient antecedent basis for this limitation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 30, 32-36, 38-39, 2-3, 5-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Shimoi et al (Mutation Research, 350 (1996) 153-161).

Shimoi discloses radioprotective effects of plant flavonoids in mammals such as mice that are subject to an ionizing radiation such as γ-radiation of 1.6 Gy. (see abstract). Thus, Shimoi meets the limitations of claims 30, 32-36. Shimoi further discusses the radioprotective components of Rooibos tea and fractionates to purify the flavonoids of interest (see page 154, sec 2). Shimoi identifies Luteolin and quercetin as the most effective flavonoids. (see sec 2.4 at page 155). Shimioi further discloses in vivo administration of such flavonoids orally via gastric intubation 6 hours prior to ionizing radiation of γ-rays. (see page 154, 1st col). Shimoi's radiation meets the instant dosing requirements encompassed in claims 2-3. Shimoi then suggests pretreatment of subjects with flavonoids. (see; page 155, 1st col; pages 157-160). Shimoi finally concludes that such flavonoids are effective radioprotectants against ionizing radiation of γ-rays. (see page 159, sec 6, 2nd para.). Accordingly, Shimoi anticipates the limitations of the instant claims.

Claims 30, 32-36, 38-39, 2-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Miller et al US Patent 6,426,362.

Miller discloses methods of ameliorating metabolism in cells secondary to external stresses such as ionizing radiation in subjects in need thereof comprising administering patients doses of flavonids such as hesperetin, diosmin or quercetin. (see col 12, lines 29-56; and claims at col 50, lines 1-15, 33-35, 50-60; col 48, lines 15-col 49, line 29). Miller also discloses formulations to contain biochanin A and Daidazin as suitable compositions for his claimed method. (see col 49, lines 30-55). Millar also

discloses various modes of in vivo delivery such as oral, intradermal, intravenous for administering his compositions to subjects in need. (see col 26, line 60-col 30, line 64).

Claims 30, 4-5, 8, stand rejected under 35 U.S.C. 102(e) as being anticipated by Lanzendorfer et al US Patent 6,423,747.

Lanzendorfer discloses methods of applying genistein to skin to reestablish the epidermal barrier function of the skin (see claims 1-5, and col 20, lines 33-36). Lanzendorfer's method related to process for protecting skin from exposures to UV rays (see col 15, line 26-40). UV rays are recognized as ionizing radiation (see col 1, lines 54-60), thus meeting the limitations of the instantly claimed radiation exposure. Therefore, Lanzendorfer anticipates the limitations of the instant claims.

Applicant's arguments with respect to this reference have been fully considered but are not persuasive. Applicant argues that Lanzendorfer does not use their compositions for treating ionizing radiation and that the reference deals with non-ionizing UV radiation. at page 8 of the response, Applicant argues that Wei reference contains a typographical error stating that UV rays are recognized as ionizing radiation citing col 1, lines 54-60. Examiner believes that this comment is directed to Lanzendorfer's patent not Wei, therefore, the response is hereby incorporated under the rejection over the Lanzendrofer reference.

First, the scope of claim 30 is directed to methods of radioprotection of a mammal. Since the claims do not narrow the mammal to such species that are "in need thereof," such treatment, the intended use is inherently provided by Lanzendorfer's methodology, as Lanzendorfer provides methods teach the instant process steps.

Second, Applicant's arguments that UV lights are not non-ionizing radiation is not founded persuasive, because applicant has failed to provide any scientific evidence or declaration showing that indeed that is UV rays are non-ionizing radiation. Given the broadest reasonable interpretation of the term "ionizing radiation" consistent with the art, Examiner views such genus to encompass any form of radiation that has enough energy to knock an electron out of atoms, molecules or a matter that it passes through, thus, creating an ion. (see Dorland's Medical Dictionary 27th ed. at Page 1404-5).

Further, to rebut Applicant's arguments, Examiner draws applicant's attention to the attached reference by Lawrence R. Coia, *Introduction to Clinical Radiation Oncology,* Medical Physics Publishing, Wisconsin, 1994, Chapter 1, "*The Physical Basis of Radiation* Oncology", pp 2-3 and figure 1.2. Accordingly, the reference indeed classifies UV (ultraviolet) rays to possess such level of energy that would classify UV rays among ionizing radiations. (see UV rays that are classified before X-rays but within the such energy level that are recognized as ionizing radiation). Examiner agrees that x-ray and γ-radiation are typical ionizing radiations, but since there are no evidence that ionizing radiations do not include UV rays in combination with the fact that Coia classifies UV rays among ionizing radiations, Examiner would maintain his position that UV radiation falls within the scope of the instantly claimed radiation. Therefore, Applicant's assertion about the typographical error in Lanzendorfer [sic Wei] is not found persuasive. Since Lanzendorfer administer their isoflavones in the same amount as instantly claimed, they inherently anticipate the limitations of the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 2-9, 18-25, 30-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimoi et al (Mutation Research, 350 (1996) 153-161) and Brown et al US Patent 6,528,042 in view of Uckun et al. (Proc. Natl. Acad. Sci. USA, 89, 9005 (1992)) and De Juan US Patent 6,399,655.

The teachings of Shimoi are described above. Shimoi only teaches for the limitation of claim 18, because its radiation would at least meet the limitation of a sub-lethal radiation dose. Shimoi only fails to explicitly describe the use of Genistein as an isoflavonoid for his methodology.

Brown teaches methods of ameliorating the disruption of energy metabolism secondary to an environmental stress such as ionizing radiation comprising administering to a subject a flavonoid within the instantly claimed ranges. (see abstract,

col 12, line 40; col 14, line 8-12; col 21, lines 55-col 22, line 65). Accordingly, Brown is viewed to alleviate or treat potential side effects caused by ionizing radiation.

Uckun supplements the teachings of Brown as it explicitly provides that genistein has been shown to prevent apoptosis in cells, which have undergone ionizing radiation or engagement of the CD19 receptor. (see abstract, and page 9008, 4-6 para.). In fact, Uckun teaches that ionizing radiation is standard therapy for B cell malignancies such as leukemia and lymphomas and that ionizing radiation stimulates B cell tyrosine kinases, triggering apoptosis and clonogenic cell death. Accordingly, Uckun concludes that tyrosine kinase inhibitors such as genistein blocked the radiation-induced tyrosine phosphorylation and apoptosis. In effect, Uckun provides ample motivation in the art to use isoflavones such as genistein to at least treat one harmful side effect of ionizing radiation.

de Juan is solely used to show that systemic application of genistein is well established in the art (cols 9-11).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to administer substitute the isoflavonoids of Shimoi with adequate doses of genistein, because as provided by Brown, Uckun, de Juan, genstein can also be administered in vivo to treat or prevent trauma caused by radiation including ionizing radiations.

Further absence of showing unexpected results there would have been no patentable difference what the source of radiation is, a radiation device or a radioactive compound, because it would have been well within ordinary level of one of skilled in the

art to employ Shimoi's methodology for providing radioprotection against radiation caused by a radioactive substance.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RUSSELL TRAVERS
PRIMARY EXAMINER
GROUP 1200